

PIPETTING METHOD AND MULTICHANNEL PIPETTING APPARATUS

SUBJECT OF THE INVENTION

The present invention relates to a pipetting method for simultaneous pipetting of a plurality
5 of sample wells or containers by means of a multichannel pipetting apparatus comprising a
pipetting unit provided with a plurality of pipetting channels, according to which method

- the pipetting channels of the multichannel pipetting unit are divided into groups, at
least some of which comprise two or more pipetting channels, and
- the pipetting tips of the pipetting unit are connected to the groups of pipetting channels
10 so that each pipetting tip communicates with all pipetting channels of a group.

In this context, pipetting refers to drawing liquid from sample wells of a micro-sample plate
or from separate containers and/or dosing liquid into sample wells of another micro-sample
plate or into separate containers.

15

STATE OF THE ART

Prior-art laboratory measuring instruments employ sample plates of many types, such as
micro-sample plates, having a standardised size such that their external dimensions are
the same while the number of sample wells varies. The traditional micro-sample plate
20 originally contained 96 sample wells in a 8 x 12 matrix. The quantity of measuring solution
needed in such a sample well is about 200 µl. To reduce the amount of measuring
solution, first a micro-sample plate having the same external dimensions and containing
384 sample wells in a 16 x 24 matrix was produced. The amount of measuring solution
needed in each well was considerably reduced, to about 50 µl. However, when a very
25 large number of samples are to be measured, it is preferable to use micro-sample plates
with still smaller sample wells. This naturally reduces the amount of measuring solution
needed. Therefore, many measuring apparatuses are nowadays implemented using micro-
sample plates containing 864 wells in a 24 x 36 matrix, in which the required amount of
solution is e.g. about 10 µl, or micro-sample plates containing 1536 wells in a 32 x 48
30 matrix, in which the required amount of solution is only about 5 µl. The number of sample
wells of the micro-sample plate may be increased still further, e.g. to 9600 sample wells in
a 80 x 120 matrix.

However, the use of many different sample plates has led to problems in laboratories
35 because for each different micro-sample plate a corresponding measuring apparatus is
needed. Different types of micro-sample plate cannot be measured crosswise in different
apparatuses. For example, a micro-sample plate containing 96 sample wells cannot be

measured in an apparatus designed for plates containing 384 sample wells, nor conversely.

Specification EP 1 074 302 A2 presents a solution for adapting a multichannel pipetting apparatus to different sample plates. It has been achieved by using pipetting tips of special construction whose upper end has been enlarged so that it connects at least two pipetting cylinders of the pipetting apparatus. If the cylinders of the multichannel pipetting apparatus are disposed at a distance from each other such that the pipetting apparatus is applicable for pipetting a sample plate containing 384 wells, then, by using pipetting tips of special construction, it is also possible to pipette a sample plate containing 96 wells. In this case, the pipetting tips selected for use in the pipetting apparatus are pipetting tips of special construction whose upper end connects four adjacent pipetting cylinders arranged side by side in a quadratic array.

The solution presented in specification EP 1 074 302 A2 is difficult because it requires many specially constructed pipetting tips with an enlarged upper end, which are difficult and expensive to manufacture. Prior-art advantageous pipetting tips can not be used in it.

OBJECT OF THE INVENTION

The object of the present invention is to disclose a method for eliminating the problems described above.

FEATURES CHARACTERISTIC OF THE INVENTION

The pipetting method of the invention is characterised in that

- groups of two or more pipetting channels are connected to pipetting tips by bringing between the pipetting channels and the pipetting tips an adapter containing several channels,
- by means of the adapter, each one of two or more groups of pipetting channels is connected to a separate pipetting tip via a channel or channel group in the adapter that is in alignment with the group,
- and that the channel or channel group in the adapter is connected to the pipetting tip, which preferably is a conventional, funnel-shaped pipetting tip.

A preferred embodiment of the pipetting method of the invention is characterised in that the adapter between the pipetting channels and the pipetting tips is replaced with a different adapter depending on the number of pipetting channels comprised in the group to be connected to each pipetting tip.

A second preferred embodiment of the pipetting method of the invention is characterised in that

the adapter placed between the pipetting channels and the pipetting tips is moved laterally
 5 so that the desired channel or channel group is brought to a position directly opposite to the selected pipetting channels, said selection being made according to the number of pipetting channels comprised in the group to be connected to each pipetting tip.

A third preferred embodiment of the pipetting method of the invention is characterised in
 10 that

by means of the adapter movable in the pipetting apparatus, the pipetting tips to be connected to the adapter are fetched according to the size of the sample wells or containers to be pipetted, whereupon the adapter is moved laterally so that the channel or channel group in the adapter which is in alignment with the pipetting tip comes to a
 15 position directly opposite to the desired group of pipetting channels, this selection being made according to the number of pipetting channels comprised in the group to be connected to each pipetting tip.

The invention also relates to a multichannel pipetting apparatus for simultaneous pipetting
 20 of a plurality of sample wells or containers, said pipetting apparatus comprising

- a pipetting unit comprising a number of pipetting channels
- in which pipetting apparatus the pipetting channels have been divided into groups, at least some of which comprise two or more pipetting channels,
- and the pipetting tips of the pipetting unit are connected to the groups of pipetting
 25 channels so that each pipetting tip communicates with all pipetting channels in a group.

The pipetting apparatus of the invention is characterised in that

- the pipetting unit of the pipetting apparatus comprises at least one adapter placed
 30 between the pipetting channels and the pipetting tips and containing a number of channels or channel groups connecting the groups of pipetting channels to the pipetting tips,
- and that each channel or channel group in the adapter is connected to one group of pipetting channels and via an orifice to one pipetting tip, which preferably is a
 35 conventional, funnel-shaped pipetting tip.

By employing the solution of the invention, a multichannel pipetting apparatus is achieved which replaces several prior-art apparatuses. A further advantage of the solution is that most embodiments of the invention can also use pipetting tips that are previously known and therefore advantageous.

5

EMBODIMENTS OF THE APPARATUS OF THE INVENTION

A preferred embodiment of the pipetting apparatus of the invention is characterised in that

- the pipetting unit comprises at least two different adapters which can be alternately placed in the pipetting unit, between the pipetting channels and the pipetting tips,
- 10 - that the adapters contain different channels or channel groups
- that the channels or channel groups in different adapters differ from each other in that a different number of pipetting channels can be connected via them to each pipetting tip.

15 A second preferred embodiment of the pipetting apparatus of the invention is characterised in that

- the pipetting unit comprises an adapter comprising at least two different zones containing different channels or channel groups,
- the channels or channel groups located in different zones of the adapter differ from
- 20 each other in that a different number of pipetting channels can be connected via them to each pipetting tip, and that
- the adapter can be displaced or moved so as to bring different zones alternately into connection with the pipetting channels.

25 A third preferred embodiment of the pipetting apparatus of the invention is characterised in that

- the pipetting apparatus comprises a track for moving micro-sample plates laterally to a position directly opposite to the pipetting unit,
- the pipetting unit contains one or more adapters which can be moved above the track
- 30 in a direction perpendicular to the direction of movement of the track, and that
- one or more adapters contain two or more different zones containing channels or channel groups which connect a different number of pipetting channels to each pipetting tip.

35 A fourth preferred embodiment of the pipetting apparatus of the invention is characterised in that

the adapter is provided with a plurality of pipetting tips (20) or pipetting tip connecting elements fixedly attached to it.

5 A fifth preferred embodiment of the pipetting apparatus of the invention is characterised in that
the channels or channel groups of the adapter are fitted against a seal on the lower surface of the frame of the pipetting unit or against suitable connecting elements.

10 Yet another preferred embodiment of the pipetting apparatus of the invention is characterised in that
the pipetting tips are fitted against a seal on the lower surface of the adapter or against suitable connecting elements.

EXAMPLES OF EMBODIMENTS

15 In the following, the invention will be described by the aid of examples with reference to the attached drawings, wherein

LIST OF DRAWINGS

- 20 Fig. 1 is a diagram representing a prior-art pipetting unit and associated pipetting tips in vertical section.
Fig. 2 corresponds to Fig. 1 and shows the pipetting tips as connected to the pipetting unit.
Fig. 3 corresponds to Fig. 1 and presents a second prior-art pipetting unit and associated pipetting tips.
25 Fig. 4 corresponds to Fig. 3 and shows the pipetting tips as connected to the pipetting unit.
Fig. 5 presents a diagrammatic vertical section of a pipetting unit according to the invention with its parts separated from each other.
Fig. 6 corresponds to Fig. 5 and presents the pipetting unit in an assembled state.
30 Fig. 7 corresponds to Fig. 5 and presents a pipetting unit according to a second embodiment of the invention with its parts separated from each other.
Fig. 8 corresponds to Fig. 7 and presents the pipetting unit in an assembled state.
Fig. 9 corresponds to Fig. 5 and presents a pipetting unit according to a third embodiment of the invention with its parts separated from each other.
35 Fig. 10 corresponds to Fig. 9 and presents the pipetting unit in an assembled state.
Fig. 11 corresponds to 5 and presents a pipetting unit according to a fourth embodiment of the invention with its parts separated from each other.

- Fig. 12 corresponds to Fig. 11 and presents the pipetting unit in an assembled state.
- Fig. 13 corresponds to 5 and presents a pipetting unit according to a fifth embodiment of the invention with its parts separated from each other.
- Fig. 14 corresponds to Fig. 13 and presents the pipetting unit in an assembled state.
- 5 Fig. 15 corresponds to Fig. 5 and presents a pipetting unit according to a sixth embodiment of the invention with its parts separated from each other.
- Fig. 16 corresponds to Fig. 15 and presents the pipetting unit in an assembled state.
- Fig. 17 corresponds to Fig. 5 and presents a pipetting unit according to a seventh embodiment of the invention with its parts separated from each other.
- 10 Fig. 18 corresponds to Fig. 17 and presents the pipetting unit in an assembled state.
- Fig. 19 presents a section taken of the unit in Fig. 5 along line XIX-XIX.
- Fig. 20 presents a section taken of the unit in Fig. 7 along line XX-XX.
- Fig. 21 presents a section taken of the unit in Fig. 9 along line XXI-XXI.
- Fig. 22 presents a section taken of the unit in Fig. 13 along line XXII-XXII.
- 15 Fig. 23 corresponds to Fig. 5 and presents a pipetting unit according to an eighth embodiment of the invention with its parts separated from each other.
- Fig. 24 presents a diagrammatic vertical section through a pipetting unit according to a ninth embodiment of the invention and its replaceable parts.
- Fig. 25 corresponds to 5 and presents a diagrammatic vertical section through a pipetting unit according to a tenth embodiment of the invention.
- 20 Fig. 26 presents a diagrammatic top view of a second pipetting apparatus according to the invention.
- Fig. 27 presents a diagrammatic lateral view of the pipetting apparatus in Fig. 26.
- Fig. 28 presents an axonometric view of a third pipetting apparatus according to the invention.
- 25 Fig. 29 presents the replaceable part of the pipetting unit according to the invention in top view.
- Fig. 30 corresponds to Fig. 29 and presents a second embodiment of the replaceable part of the pipetting unit in top view.
- 30 Fig. 31 presents a diagram visualising the layout of the flow channels of the pipetting unit of the invention.
- Fig. 32 corresponds to Fig. 29 and presents a top view of a third embodiment of the replaceable part of the pipetting unit.
- Fig. 33 presents a diagrammatic vertical section of a pipetting unit according to an eleventh embodiment of the invention.
- 35 Fig. 34 corresponds to 33 and presents the pipetting unit in another position.

DESCRIPTION OF THE DRAWINGS

Fig. 1 shows a vertical section of a prior-art pipetting unit 10 with a frame part 16 containing a plurality of dosage cylinders 12 provided with pistons 11. The pipetting tips 20 are brought into the pipetting unit 10 as a group placed in a support plate 21, so that all the pipetting tips 20 can be connected simultaneously to the dosage orifices 13 of the pipetting unit 10. The lower surface of the frame 16 of the pipetting unit 10 is provided with a rubber seal 14 for sealing the joint between the dosage orifices 13 and the pipetting tips 20 pressed against the seal 14.

In Fig. 2, the pipetting tips 20 placed in the support plate 21 have been connected to the pipetting unit 10. After this, using the pipetting tips 20 of the pipetting unit 10, liquid is drawn by suction from the sample wells of a first micro-sample plate or from separate containers and dosed into the sample wells of a second micro-sample plate or into separate containers. To draw liquid into the pipetting tip 20, the piston 11 of the dosage cylinder 12 in the frame 16 of the pipetting unit 10 is moved upward, thus producing a negative pressure in the air space of the dosage cylinder 12. The liquid being pipetted now rises into the pipetting tip 20. Dosage is performed in reverse order by moving the piston 11 of the dosage cylinder 12 in the pipetting unit 10 downward, causing the liquid being dosed to be correspondingly removed from the pipetting tip 20.

To allow simultaneous dosage by a plurality of pipetting tips 20, the pipetting tips 20 in the pipetting unit 10 have to be arranged in the same way as the sample wells or separate containers used as pipetting sources. Similarly, the pipetting tips 20 have to be disposed at the same distances between them as the sample wells or separate containers used as pipetting sources.

After this, the liquid can be dosed into the sample wells or separate containers in another sample plate which have been arranged in the way as the sample wells or separate containers use as pipetting sources. The receiving sample wells also have to be disposed at the same distances between them as the sample wells or separate containers used as pipetting sources.

However, if the pipetting tips 20 are sufficiently narrow, then the liquid can also be dosed into the sample wells in another sample plate in which the wells are disposed at distances equalling only half the distances between the sample wells used as pipetting sources. In this case, pipetting is performed by first dosing the liquid into every second sample well in the other sample plate and then into the sample wells that were left between said every

second well during the first pipetting operation. These two dosage operations have to be performed both in the widthways direction and in the lengthways direction of the sample plate, so this sample plate containing a quadruple number of sample wells can be filled via four dosage operations.

5

In the manner described above, using a prior-art pipetting apparatus with a pipetting unit containing 24 pipetting tips, it is possible to dose liquid from 24 sample containers or from a sample plate containing 24 sample wells into another micro-sample plate containing 24 or 96 sample wells. Similarly, using another prior-art pipetting apparatus with a pipetting
 10 unit containing 96 pipetting tips, it is possible to pipette from a micro-sample plate containing 96 sample wells into another micro-sample plate containing 96 or 384 sample wells.

However, using prior-art apparatus, it is difficult to pipette e.g. from a sample plate
 15 containing 24 sample wells into a micro-sample plate containing 384 sample wells. This is generally due to the fact that pipetting tips designed for larger sample wells are too large to be inserted into smaller sample wells. Obviously enough, 384 sample wells accommodated in a sample plate of the same size must be considerably smaller than e.g. the sample wells in a micro-sample plate containing 96 sample wells. Therefore, it is generally likewise
 20 impossible to pipette from a micro-sample plate containing 96 sample wells into another micro-sample plate containing 1536 sample wells. It is true that pipetting can be performed using pipetting tips that are small enough to be inserted into small sample wells. In this case, however, there is the problem that the pipetting tips can only contain such a small amount of liquid that filling larger sample wells is a very slow operation. The pipetting
 25 would have to be repeated several times. Therefore, in current practice several pipetting units of different sizes are needed to enable dosage operations as described above to be carried out efficiently.

Fig. 3 presents another prior-art pipetting unit 10 which also uses separate pipetting tips
 30 20. The pipetting tips 20 are pressed into connecting elements 15 placed opposite to the dosage cylinders 12 in the frame 16 of the pipetting unit 10. In this example, the connecting elements 15 and the pipetting tips 20 are so closely fitted that no separate seals are needed. However, there are many different ways of connecting the pipetting tips 20a, including solutions in which one or more seals, such as e.g. O-rings, are used.

35

The pipetting tips 20 in Fig. 3 can be pressed into the connecting elements 15 one at a time or by using a separate pipetting tip holder, either manually or mechanically. In Fig. 4, the pipetting tips 20 have been connected to the pipetting unit 10.

5 Fig. 5 presents a pipetting unit 10 according to the invention, which is substantially different from prior-art structures. The operation of the assembly presented in Fig. 5 does not in itself differ from the operation of previously known apparatuses, but this pipetting unit 10 forms part of a configuration the various details of which will be described in connection with the following figures. The pipetting unit 10 in Fig. 5 comprises an adapter
10 30a placed between the dosage cylinders 12 in the frame 16 and the pipetting tips 20a, which adapter forms an essential part of the pipetting unit 10 of the invention. The adapter 30a is provided with channels 31a through which the dosage orifices 13 of the dosage cylinders 1 communicate with the pipetting tips 20. Fig. 5 shows that in this example embodiment of the pipetting unit 10 of the invention, the numbers of dosage orifices 13 of
15 dosage cylinders 12, channels 31a and pipetting tips 20 are the same.

The lower surface of the adapter 30a is provided with a seal 14b which is identical to the seal 14 on the lower surface of the pipetting unit 10. Thus, both the joint between the adapter 30a and the frame 16 of the pipetting unit 10 and the joint between the implement
20 and the pipetting tips 20a are sealed. Fig. 5 also shows that the pipetting tips 20a and their support plate 21a are identical to those in the prior-art pipetting unit 10 presented Fig. 1 and 2. In other words, known standard-type pipetting tips can be used in this embodiment of the pipetting unit 10 of the invention. Fig. 6 presents a pipetting unit 10 according to the invention in an assembled state and ready for use. The inventive significance of the
25 adapter 30a is described in connection with the following figures.

Fig. 7 presents a second embodiment of the pipetting unit 10 of the invention in which the difference from previously known solutions can be clearly seen. The essential point is that a completely different adapter 30b has been connected to a pipetting unit 10 frame 16 like
30 that presented in Fig. 6. The difference between adapter 30b and the adapter 30a presented in Fig. 6 is that, as can be seen from the cross-sectional view in Fig. 7, channels 31b connect the dosage orifices 13 of two dosage cylinders 12 to one larger orifice 32b, which in turn is connected to a pipetting tip 20b of a conventional type. The channels 31b in the adapter 30b connect two dosage cylinder 12 dosage orifices 13 in both widthways
35 and lengthways directions of the adapter 30b, each pipetting tip 20b being thus connected to four dosage cylinder 12 dosage orifices 13, as is later shown in a sectional view in Fig. 20.

Fig. 8 presents the pipetting unit 10 of Fig. 7 in an assembled state. In the embodiments in Fig. 7 and 8, the pipetting unit 10 and its frame 16 may be the same as in the previous figures, in other words, the apparatus is a pipetting unit 10 known in itself in which only an adapter 30b according to the invention has been changed. At the same time, the adapter 30b has been fitted with larger pipetting tips 20b, which, however, may also consist of existing, i.e. known standard-type pipetting tips 20b. The essential point about the solutions presented in Fig. 5-8 is that, by using different adapters 30a and 30b, the known basic part 16 of a pipetting unit 10 and known pipetting tips 20b can be used in considerably more versatile ways than before. In other words, a simple solution enables a single apparatus to function like two or more prior-art apparatuses together.

Fig. 9 presents yet another variation of the solutions presented in Fig. 5-8. In this case, a channel 31c in the third adapter 30c according to the invention connects the dosage orifices 13 of four dosage cylinders 12 in a cross-sectional view to a larger orifice 32c, which again is connected to a pipetting tip 20c of conventional type. Here, too, it is to be noted that the channels 31c in the adapter 30c connect four dosage cylinder 12 dosage orifices 13 in both widthways and lengthways directions of the adapter 30c, each pipetting tip 20c being thus connected to sixteen dosage cylinder 12 dosage orifices 13, as is later shown in the cross-sectional view in Fig. 21. Fig. 10 presents the pipetting unit 10 of Fig. 9 in an assembled state.

In a way, the pipetting units 10 presented in Fig. 6-10 form part of the same entity, in which the basic part of the pipetting unit 10 and the frame 16 comprised in it and containing the dosage cylinders is the same in all these figures. Thus, by only changing the adapter 30 and the associated individual pipetting tips 20 known in themselves, pipetting can be performed efficiently between micro-sample plates or corresponding separate containers of widely varying sizes.

As generally a single pipetting tip size is well applicable for pipetting two or three different-sized sample wells, it is possible, by alternately using apparatuses as presented in Fig. 6-10, to pipette efficiently and quickly at least 6-7 differently sized sample wells by means of three pipetting tips 20a-20c of different sizes. In practice, this is enough to allow pipetting of all sample wells of different sizes needed in laboratory work. However, if a still wider range of application is required, then, according to the invention, the number of adapters 30 used in the pipetting unit 10 can be increased still further.

Fig. 11 and 12 present an embodiment comprising a pipetting unit 10 and channels 31d in an adapter 30d which in the cross-sectional view connect two dosage cylinders 12 to one orifice 32d and further to a pipetting tip 20d. As in the embodiment in Fig. 7, the channels 31d connect two dosage cylinders 12 in both widthways and lengthways directions of the adapter 30d. Each pipetting tip 20d is thus connected to four dosage cylinders 12.

As a difference from Fig. 7, the channels 31d in the adapter 30d in Fig. 11 and 12 are fitted directly without separate seals to the connecting elements 15a added to the frame 16. The orifices 32d in the adapter 30d are provided with corresponding connecting elements 15b for the pipetting tips 20d.

Fig. 13 and 14 present an embodiment in which the adapter 30e is provided with channels 31e which in the cross-sectional view connect four dosage cylinders 12, i.e. in the widthways and lengthways directions a total of sixteen dosage cylinders 12 to one orifice 32e and further to a pipetting tip 20e of a known type. In this embodiment, too, the adapter 30e can be connected via the orifices of the channels 31e to the connecting elements 15a of the frame 16 of the pipetting unit 10 without separate seals. Similarly, a conventional pipetting tip 20e can be connected to the connecting element 15e of the adapter 30e without separate seals. A sectional view of this adapter 30e is presented in Fig. 22.

The solutions presented in Fig. 10-14 are also in a way part of the same entity in which different adapters 30 and pipetting tips 20, conventional in themselves but of different sizes, connected to them can be used in connection with the basic part of the pipetting unit 10 and its frame 16. In this way, a very wide range of use of the same multichannel pipetting apparatus is achieved in the pipetting of sample wells of different sizes.

Fig. 15 and 16 present an embodiment of a pipetting unit 10 in which the upper surface of the adapter 30f is provided with a seal 14f. In this case, the adapter 30f can be fitted tightly against the lower surface 17 of the frame 16 of the pipetting unit 10 as an alternative to connection to connecting elements 15a, which was the case in the previous example. In this example, one large common channel 31f connects four adjacent dosage cylinders 12 arranged in a quadratic array to a single orifice 32f.

The adapter 30f can also be varied in numerous other ways by combining different types of joint at its upper and lower surfaces. The drawings and this description do not present all these alternatives. For example, the lower surface of adapter 30f may be straight as in Fig. 7 and provided with a seal 14 instead of connecting elements 15f. In this case, in place of

pipetting tips 20d, there will be standard-type pipetting tips 20b together with a support plate 21b, as in Fig. 7.

Fig. 17 and 18 present a solution resembling the one presented in Fig. 15 and 16, likewise with a seal 14g on the upper surface of the adapter 30g. The difference in this example is that, instead of connecting four dosage cylinders 12 of the frame 16 of the pipetting unit 10, one large common channel 31g connects sixteen dosage cylinders 12 to an orifice 32e in the adapter 30g and further to a pipetting tip 20e of a known type.

Fig. 19-22 present horizontal sections through certain alternative adapters 30a, 30b, 30c and 30e. In the adapter 30a in Fig. 19, each channel 31a connects only one dosage cylinder directly to one pipetting tip, as shown in Fig. 5 and 6.

In the adapter 30b in Fig. 20, each channel 31b connects four dosage cylinders 12 in the frame 16 of the pipetting unit 10 to one orifice 32b in the adapter 30b and further to a pipetting tip 20e of a known type as shown in Fig. 7 and 8.

In the adapter 30c in Fig. 21, a large common channel 31c connects sixteen dosage cylinders of the pipetting unit 10, arranged in a quadratic array, to one orifice 32c and further to a pipetting tip of a known type. A vertical section of a corresponding pipetting unit is presented in Fig. 9 and 10.

The adapter 30e in Fig. 22 contains several small channels 31e which also connect sixteen dosage cylinders of the pipetting unit 10 to one orifice 32e and further to a pipetting tip of a known type as in the previous figure. However, there is a difference in the structure of the channel system, in which, instead of a single large space, several small channels are connected to the orifice 32e. A vertical section of a pipetting unit 10 corresponding to this embodiment is shown in Fig. 13 and 14.

Fig. 23 presents a pipetting unit 10 with an adapter 30b like that in Fig. 7 and 8. However, the frame 16 of the pipetting unit 10 differs in that the dosage cylinders are located at a distance from the adapter 30b. The dosage cylinders, which are not shown in Fig. 23, are connected via tubes 18 to the dosage orifices 13 of the frame 16.

Fig. 24 presents a pipetting unit 10 to whose frame 16 it is possible to alternatively connect one of three different adapters 30 provided with fixed pipetting tips 23 or with separate pipetting tips 20a placed over them. The adapter 30h in Fig. 24a has one fixed pipetting tip

for each dosage cylinder 12 of the pipetting unit 10. The adapter 30i in Fig. 24b again has one fixed pipetting tip 23i or a separate pipetting tip 20b placed over it for four dosage cylinders 12 of the pipetting unit 10. The adapter 30j in Fig. 24c again has one fixed pipetting tip 23j or a separate pipetting tip 20c placed over it for sixteen dosage cylinders
 5 12 of the pipetting unit 10. In the embodiments presented in Fig. 24, fixed pipetting tips 23 can be used e.g. when the apparatus is mainly used for only dosing a liquid. To transfer a liquid from a sample plate to another by pipetting, it is generally necessary to use replaceable separate tips 20.

10 Fig. 25 presents a pipetting unit 10 in which the frame 16 is connected to a laterally movable adapter 30k provided with different fixed pipetting tips 23 or with separate pipetting tips 20 placed over them. The adapter 30k can be moved laterally so that either zone 22a, 22b or 22c of the adapter 30k comes to the position directly opposite to the dosage orifices 13 of the dosage cylinders.

15 In zone 22a of the adapter 30k, each dosage cylinder dosage orifice 13 is aligned with a channel 31h which leads to a fixed pipetting tip 23a or a separate pipetting tip 20a placed over it, likewise aligned with the orifice.

In zone 22b of the adapter 30k, there is a connecting channel 31i, an orifice 32i and a fixed
 20 pipetting tip 23b or a separate pipetting tip 20b placed over it for four dosage cylinders 12 of the pipetting unit 10. Zone 22c of the adapter 30k again has a connecting channel 31j, an orifice 32j and a fixed pipetting tip 23c or a separate pipetting tip 20c placed over it for sixteen dosage cylinders 12 of the pipetting unit 10.

25 The pipetting process can be varied depending on the type of micro-sample plate under pipetting simply by moving one of the zones 22a, 22b or 22c of the adapter 30k to the position directly opposite to the dosage orifices 13 of the dosage cylinders of the pipetting unit 10. As described above, the pipetting tips in this embodiment are fixedly joined to the adapter 30k. Alternatively, it is naturally also possible to use separate, preferably standard-
 30 type pipetting tips either in addition to the fixed pipetting tips 23, e.g. by placing them over these, or instead of these. When separate pipetting tips 20 are used, the apparatus can also be so implemented that either the measuring head of the pipetting unit 10 or the movable adapter 30k fetches new pipetting tips when necessary.

35 Using the pipetting unit 10 in Fig. 25, the pipetting of the sample wells of a sample plate can be carried out by selecting from the adapter 30k pipetting tips 20 or 23 of the most suitable size for each pipetting situation. Thus, using this pipetting apparatus, large sample

wells can be pipetted using large pipetting tips, and when smaller sample wells need to be pipetted, smaller pipetting tips are applied as necessary. Since all the required pipetting tips of different sizes are present in the pipetting apparatus all the time, the apparatus works very efficiently and fast as compared with prior-art apparatuses and methods.

5

Fig. 26 presents a diagrammatic top view of a pipetting apparatus 40 according to the invention. The pipetting apparatus 40 comprises a pipetting unit 10 and a track 41 for feeding and moving micro-sample plates 42 in lateral directions to bring them to a position directly opposite to the pipetting unit 10. The pipetting unit 10 also comprises an adapter 30 which can be moved laterally but also perpendicularly to the movement of the track 41 and which contains several pipetting tip groups 22 consisting of pipetting tips of different sizes. The adapter 30 is moved laterally so as to bring a desired pipetting tip group 22 to the active position directly opposite to the pipetting unit 10. The pipetting tip group 22 is selected by the type of the micro-sample plate 42 brought on the track 41 to the position opposite to the pipetting unit 10 and by the number of sample wells 44 in the sample plate.

10
15

As the track 41 of the micro-sample plates 42 and the movements of the adapter 30 of the pipetting unit 10 are independent from each other, these movements can be controlled so as to bring any one of the pipetting tip groups and micro-sample plates to the pipetting unit 10 for pipetting. In other words, all possible combinations are feasible. The essential point about the apparatus is not whether the pipetting tips are fixedly or detachably mounted in the adapter 30. In practice, naturally the most advantageous alternative is to use separate standard-type pipetting tips. In the apparatus in Fig. 26, it is also possible to use an arrangement whereby the apparatus also fetches new pipetting tips into the adapter 30 as necessary.

20
25

Fig. 27 presents the pipetting apparatus 40 of Fig. 26 in side view. The figure shows a pipetting unit 10 and an adapter 30 and below them a track 41 for feeding and moving micro-sample plates 42 laterally to the position opposite to the pipetting unit 10. The adapter 30 moves in a direction perpendicular to the movement of the track 41, i.e. in a direction away from the plane of the drawing.

30

Fig. 28 presents a pipetting apparatus 40 which is a simplified version of the apparatus presented in Fig. 26 and 27, and in which the micro-sample plates 42 are fed onto the track 41 from a feed device 43. The pipetting unit 10 above the track 41 is provided with a movable adapter 30 with three replaceable pipetting tip groups 22. The pipetting unit 10

35

can fetch a new group to replace a pipetting tip group 22 when necessary. The pipetting tips may be fixed or separate tips.

Fig. 29 presents a more detailed view of a replaceable adapter 30a containing 384
 5 channels 31a. It is intended for pipetting a known micro-sample plate containing 384
 sample wells, in which the sample wells are arranged in the same order as the channels
 31a in the adapter 30a. The dosage cylinders above the adapter 30a are also spaced at
 the same distances between them as the channels 31a of the adapter 30a and the
 pipetting tips and sample wells of the micro-sample plate below them. Thus, each dosage
 10 cylinder is connected via one channel 31a of the adapter 30a to one pipetting tip aligned
 with the sample well.

Fig. 30 also shows a more detailed view of another replaceable adapter 30b of the pipetting
 unit 10, containing 96 connecting channels 31b of another type. If the adapter 30a in the
 15 pipetting unit in Fig. 29 is replaced with this adapter 31b, then each connecting channel 31b
 connects four dosage cylinders of the pipetting unit via an orifice 32 to one larger, standard-
 type pipetting tip. In this case, the distance between these larger pipetting tips corresponds
 to the distance between the sample wells of a micro-sample plate containing 96 sample
 wells.

20 Fig. 31 shows in a diagrammatic form how a replaceable adapter 30b of the pipetting unit
 10 as presented in Fig. 30 connects four dosage cylinder dosage orifices to one dosage
 orifice 32b in the adapter 30, which again can be connected to a standard-type pipetting
 tip. In each group of four dosage orifices, the orifice 32b to the pipetting tip is placed in the
 middle of the group. By means of this adapter 30b, using a pipetting unit containing 384
 25 dosage cylinders, a micro-sample plate containing 96 sample wells can be pipetted. Again,
 by replacing the adapter in the pipetting unit with an adapter 30a as presented in Fig. 29, a
 micro-sample plate containing 384 sample wells can be pipetted.

30 Fig. 32 presents an example of the laterally movable adapter 30 of the pipetting unit 10.
 This adapter 30 comprises two zones 22a and 22b, of which the first zone 22a contains
 only direct channels 31a while the second zone 22b contains only channels 31b
 connecting four dosage cylinder dosage orifices to one orifice 32b. The adapter 30 in Fig.
 32 may alternatively be formed by disposing the zones 22a and 22b with their longer sides
 35 contiguous to each other. In principle, the adapter 30 may also comprise any number of
 zones 22 combined in any order.

Fig. 33 presents as an example a lateral view of a pipetting unit 10 provided with a laterally movable adapter 30 as shown in Fig. 32. In Fig. 33, the adapter 30 is in a position such that the dosage orifices of the dosage cylinders 12 are aligned with the direct channels 31a.

5

In Fig. 34 again, the laterally movable adapter 30 of the pipetting unit 10 is in a position such that the dosage orifices of the dosage cylinders 12 are aligned with the channels 31b connecting four dosage cylinder dosage orifices.

10 ADDITIONAL REMARKS

It is obvious to the person skilled in the art that different embodiments of the invention may be varied within the scope of the claims presented below.

11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000
1001
1002
1003
1004
1005
1006
1007
1008
1009
1010
1011
1012
1013
1014
1015
1016
1017
1018
1019
1020
1021
1022
1023
1024
1025
1026
1027
1028
1029
1030
1031
1032
1033
1034
1035
1036
1037
1038
1039
1040
1041
1042
1043
1044
1045
1046
1047
1048
1049
1050
1051
1052
1053
1054
1055
1056
1057
1058
1059
1060
1061
1062
1063
1064
1065
1066
1067
1068
1069
1070
1071
1072
1073
1074
1075
1076
1077
1078
1079
1080
1081
1082
1083
1084
1085
1086
1087
1088
1089
1090
1091
1092
1093
1094
1095
1096
1097
1098
1099
1100
1101
1102
1103
1104
1105
1106
1107
1108
1109
1110
1111
1112
1113
1114
1115
1116
1117
1118
1119
1120
1121
1122
1123
1124
1125
1126
1127
1128
1129
1130
1131
1132
1133
1134
1135
1136
1137
1138
1139
1140
1141
1142
1143
1144
1145
1146
1147
1148
1149
1150
1151
1152
1153
1154
1155
1156
1157
1158
1159
1160
1161
1162
1163
1164
1165
1166
1167
1168
1169
1170
1171
1172
1173
1174
1175
1176
1177
1178
1179
1180
1181
1182
1183
1184
1185
1186
1187
1188
1189
1190
1191
1192
1193
1194
1195
1196
1197
1198
1199
1200
1201
1202
1203
1204
1205
1206
1207
1208
1209
1210
1211
1212
1213
1214
1215
1216
1217
1218
1219
1220
1221
1222
1223
1224
1225
1226
1227
1228
1229
1230
1231
1232
1233
1234
1235
1236
1237
1238
1239
1240
1241
1242
1243
1244
1245
1246
1247
1248
1249
1250
1251
1252
1253
1254
1255
1256
1257
1258
1259
1260
1261
1262
1263
1264
1265
1266
1267
1268
1269
1270
1271
1272
1273
1274
1275
1276
1277
1278
1279
1280
1281
1282
1283
1284
1285
1286
1287
1288
1289
1290
1291
1292
1293
1294
1295
1296
1297
1298
1299
1300
1301
1302
1303
1304
1305
1306
1307
1308
1309
1310
1311
1312
1313
1314
1315
1316
1317
1318
1319
1320
1321
1322
1323
1324
1325
1326
1327
1328
1329
1330
1331
1332
1333
1334
1335
1336
1337
1338
1339
1340
1341
1342
1343
1344
1345
1346
1347
1348
1349
1350
1351
1352
1353
1354
1355
1356
1357
1358
1359
1360
1361
1362
1363
1364
1365
1366
1367
1368
1369
1370
1371
1372
1373
1374
1375
1376
1377
1378
1379
1380
1381
1382
1383
1384
1385
1386
1387
1388
1389
1390
1391
1392
1393
1394
1395
1396
1397
1398
1399
1400
1401
1402
1403
1404
1405
1406
1407
1408
1409
1410
1411
1412
1413
1414
1415
1416
1417
1418
1419
1420
1421
1422
1423
1424
1425
1426
1427
1428
1429
1430
1431
1432
1433
1434
1435
1436
1437
1438
1439
1440
1441
1442
1443
1444
1445
1446
1447
1448
1449
1450
1451
1452
1453
1454
1455
1456
1457
1458
1459
1460
1461
1462
1463
1464
1465
1466
1467
1468
1469
1470
1471
1472
1473
1474
1475
1476
1477
1478
1479
1480
1481
1482
1483
1484
1485
1486
1487
1488
1489
1490
1491
1492
1493
1494
1495
1496
1497
1498
1499
1500
1501
1502
1503
1504
1505
1506
1507
1508
1509
1510
1511
1512
1513
1514
1515
1516
1517
1518
1519
1520
1521
1522
1523
1524
1525
1526
1527
1528
1529
1530
1531
1532
1533
1534
1535
1536
1537
1538
1539
1540
1541
1542
1543
1544
1545
1546
1547
1548
1549
1550
1551
1552
1553
1554
1555
1556
1557
1558
1559
1560
1561
1562
1563
1564
1565
1566
1567
1568
1569
1570
1571
1572
1573
1574
1575
1576
1577
1578
1579
1580
1581
1582
1583
1584
1585
1586
1587
1588
1589
1590
1591
1592
1593
1594
1595
1596
1597
1598
1599
1600
1601
1602
1603
1604
1605
1606
1607
1608
1609
1610
1611
1612
1613
1614
1615
1616
1617
1618
1619
1620
1621
1622
1623
1624
1625
1626
1627
1628
1629
1630
1631
1632
1633
1634
1635
1636
1637
1638
1639
1640
1641
1642
1643
1644
1645
1646
1647
1648
1649
1650
1651
1652
1653
1654
1655
1656
1657
1658
1659
1660
1661
1662
1663
1664
1665
1666
1667
1668
1669
1670
1671
1672
1673
1674
1675
1676
1677
1678
1679
1680
1681
1682
1683
1684
1685
1686
1687
1688
1689
1690
1691
1692
1693
1694
1695
1696
1697
1698
1699
1700
1701
1702
1703
1704
1705
1706
1707
1708
1709
1710
1711
1712
1713
1714
1715
1716
1717
1718
1719
1720
1721
1722
1723
1724
1725
1726
1727
1728
1729
1730
1731
1732
1733
1734
1735
1736
1737
1738
1739
1740
1741
1742
1743
1744
1745
1746
1747
1748
1749
1750
1751
1752
1753
1754
1755
1756
1757
1758
1759
1760
1761
1762
1763
1764
1765
1766
1767
1768
1769
1770
1771
1772
1773
1774
1775
1776
1777
1778
1779
1780
1781
1782
1783
1784
1785
1786
1787
1788
1789
1790
1791
1792
1793
1794
1795
1796
1797
1798
1799
1800
1801
1802
1803
1804
1805
1806
1807
1808
1809
1810
1811
1812
1813
1814
1815
1816
1817
1818
1819
1820
1821
1822
1823
1824
1825
1826
1827
1828
1829
1830
1831
1832
1833
1834
1835
1836
1837
1838
1839
1840
1841
1842
1843
1844
1845
1846
1847
1848
1849
1850
1851
1852
1853
1854
1855
1856
1857
1858
1859
1860
1861
1862
1863
1864
1865
1866
1867
1868
1869
1870
1871
1872
1873
1874
1875
1876
1877
1878
1879
1880
1881
1882
1883
1884
1885
1886
1887
1888
1889
1890
1891
1892
1893
1894
1895
1896
1897
1898
1899
1900
1901
1902
1903
1904
1905
1906
1907
1908
1909
1910
1911
1912
1913
1914
1915
1916
1917
1918
1919
1920
1921
1922
1923
1924
1925
1926
1927
1928
1929
1930
1931
1932
1933
1934
1935
1936
1937
1938
1939
1940
1941
1942
1943
1944
1945
1946
1947
1948
1949
1950
1951
1952
1953
1954
1955
1956
1957
1958
1959
1960
1961
1962
1963
1964
1965
1966
1967
1968
1969
1970
1971
1972
1973
1974
1975
1976
1977
1978
1979
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
2025
2026
2027
2028
2029
2030
2031
2032
2033
2034
2035
2036
2037
2038
2039
2040
2041
2042
2043
2044
2045
2046
2047
2048
2049
2050
2051
2052
2053
2054
2055
2056
2057
2058
2059
2060
2061
2062
2063
2064
2065
2066
2067
2068
2069
2070
2071
2072
2073
2074
2075
2076
2077
2078
2079
2080
2081
2082
2083
2084
2085
2086
2087
2088
2089
2090
2091
2092
2093
2094
2095
2096
2097
2098
2099
2100
2101
2102
2103
2104
2105
2106
2107
2108
2109
2110
2111
2112
2113
2114
2115
2116
2117
2118
2119
2120
2121
2122
2123
2124
2125
2126
2127
2128
2129
2130
2131
2132
2133
2134
2135
2136
2137
2138
2139
2140
2141
2142
2143
2144
2145
2146
2147
2148
2149
2150
2151
2152
2153
2154
2155
2156
2157
2158
2159
2160
2161
2162
2163
2164
2165
2166
2167
2168
2169
2170
2171
2172
2173
2174
2175
2176
2177
2178
2179
2180
2181
2182
2183
2184
2185